gastrointestinal stromal tumor

A gastrointestinal stromal tumor (GIST) is a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine. The tumors are thought to grow from specialized cells found in the gastrointestinal tract called interstitial cells of Cajal (ICCs) or precursors to these cells. GISTs are usually found in adults between ages 40 and 70; rarely, children and young adults develop these tumors. The tumors can be cancerous (malignant) or noncancerous (benign).

Small tumors may cause no signs or symptoms. However, some people with GISTs may experience pain or swelling in the abdomen, nausea, vomiting, loss of appetite, or weight loss. Sometimes, tumors cause bleeding, which may lead to low red blood cell counts (anemia) and, consequently, weakness and tiredness. Bleeding into the intestinal tract may cause black and tarry stools, and bleeding into the throat or stomach may cause vomiting of blood.

Affected individuals with no family history of GIST typically have only one tumor (called a sporadic GIST). People with a family history of GISTs (called familial GISTs) often have multiple tumors and additional signs or symptoms, including noncancerous overgrowth (hyperplasia) of other cells in the gastrointestinal tract and patches of dark skin on various areas of the body. Some affected individuals have a skin condition called urticaria pigmentosa (also known as cutaneous mastocytosis), which is characterized by raised patches of brownish skin that sting or itch when touched.

Frequency

Approximately 5,000 new cases of GIST are diagnosed in the United States each year. However, GISTs may be more common than this estimate because small tumors may remain undiagnosed.

Genetic Changes

Genetic changes in one of several genes are involved in the formation of GISTs. About 80 percent of cases are associated with a mutation in the *KIT* gene, and about 10 percent of cases are associated with a mutation in the *PDGFRA* gene. Mutations in the *KIT* and *PDGFRA* genes are associated with both familial and sporadic GISTs. A small number of affected individuals have mutations in other genes.

The *KIT* and *PDGFRA* genes provide instructions for making receptor proteins that are found in the cell membrane of certain cell types and stimulate signaling pathways inside the cell. Receptor proteins have specific sites into which certain other proteins, called ligands, fit like keys into locks. When the ligand attaches (binds), the KIT or PDGFRA receptor protein is turned on (activated), which leads to activation of a series of proteins

in multiple signaling pathways. These signaling pathways control many important cellular processes, such as cell growth and division (proliferation) and survival.

Mutations in the *KIT* and *PDGFRA* genes lead to proteins that no longer require ligand binding to be activated. As a result, the proteins and the signaling pathways are constantly turned on (constitutively activated), which increases the proliferation and survival of cells. When these mutations occur in ICCs or their precursors, the uncontrolled cell growth leads to GIST formation.

Inheritance Pattern

Most cases of GIST are not inherited. Sporadic GIST is associated with somatic mutations, which are genetic changes that occur only in the tumor cells and occur during a person's lifetime.

In some cases of familial GIST, including those associated with mutations in the *KIT* and *PDGFRA* genes, mutations are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase a person's chance of developing tumors.

When familial GIST is associated with mutations in other genes, it can have an autosomal recessive pattern of inheritance, which means alterations in both copies of the gene in each cell increase a person's chance of developing tumors.

Other Names for This Condition

- gastrointestinal stromal neoplasm
- gastrointestinal stromal sarcoma
- GIST

Diagnosis & Management

Formal Diagnostic Criteria

- Canadian Medical Association Clinical Practice Guidelines Database: Gastrointestinal Stromal Tumours (GIST) (Alberta Health Services) http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-sar002-gist.pdf

Formal Treatment/Management Guidelines

- Canadian Medical Association Clinical Practice Guidelines Database: Gastrointestinal Stromal Tumours (GIST) (Alberta Health Services) http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-sar002-gist.pdf
- National Guideline Clearinghouse: Imatinib for the Adjuvant Treatment of Gastrointestinal Stromal Tumours (Review of NICE Technology Appraisal Guidance 196) (National Institute for Health and Care Excellence) https://www.guideline.gov/summaries/summary/48876/imatinib-for-the-adjuvant-treatment-of-gastrointestinal-stromal-tumours-review-of-nice-technology-appraisal-guidance-196?q=gastrointestinal+stromal+tumor

Genetic Testing

- Genetic Testing Registry: Gastrointestinal stromal tumor https://www.ncbi.nlm.nih.gov/gtr/conditions/C0238198/

Other Diagnosis and Management Resources

- American Cancer Society: Treating Gastrointestinal Stromal Tumor (GIST) https://www.cancer.org/cancer/gastrointestinal-stromal-tumor/treating/by-spread.html
- Cancer.Net: Gastrointestinal Stromal Tumor--Diagnosis http://www.cancer.net/cancer-types/gastrointestinal-stromal-tumor-gist/diagnosis?sectionTitle=Diagnosis

General Information from MedlinePlus

- Diagnostic Tests https://medlineplus.gov/diagnostictests.html
- Drug Therapy https://medlineplus.gov/drugtherapy.html
- Genetic Counseling https://medlineplus.gov/geneticcounseling.html
- Palliative Care https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Urticaria Pigmentosa
  https://medlineplus.gov/ency/article/001466.htm
- Health Topic: Intestinal Cancer
  https://medlineplus.gov/intestinalcancer.html

Genetic and Rare Diseases Information Center

- Gastrointestinal Stromal Tumors
  https://rarediseases.info.nih.gov/diseases/8598/gastrointestinal-stromal-tumors

Educational Resources

- American Cancer Society: What is Gastrointestinal Stromal Tumor (GIST)?
  https://www.cancer.org/cancer/gastrointestinal-stromal-tumor/about/what-is-gist.html
- Disease InfoSearch: Gastrointestinal Stromal Tumors
  http://www.diseaseinfosearch.org/Gastrointestinal+Stromal+Tumors/2997
- GIST Support International (GSI): Familial GIST
  http://www.gistsupport.org/about-gist/familial-gist.php
- GIST Support International (GSI): Mutation Analysis: Kit and PDGFRA
  http://www.gistsupport.org/about-gist/mutation-analysis-kit-and-pdgfra.php
- MalaCards: gastrointestinal stromal tumor
  http://www.malacards.org/card/gastrointestinal_stromal_tumor
- Orphanet: Gastrointestinal stromal tumor
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=44890

Patient Support and Advocacy Resources

- American Cancer Society
  https://www.cancer.org/
- GIST Support International (GSI)
  http://www.gistsupport.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/gastrointestinal-stromal-tumors/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22gastrointestinal+stromal+tumor%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Gastrointestinal+Stromal+Tumor%5BTI%5D%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- GASTROINTESTINAL STROMAL TUMOR
  http://omim.org/entry/606764

Sources for This Summary

- Agaram NP, Wong GC, Guo T, Maki RG, Singer S, Dematteo RP, Besmer P, Antonescu CR. Novel V600E BRAF mutations in imatinib-naive and imatinib-resistant gastrointestinal stromal tumors. Genes Chromosomes Cancer. 2008 Oct;47(10):853-9. doi: 10.1002/gcc.20589.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18615679
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2902874/
- Heinrich MC, Corless CL, Duensing A, McGreevey L, Chen CJ, Joseph N, Singer S, Griffith DJ, Haley A, Town A, Demetri GD, Fletcher CD, Fletcher JA. PDGFRA activating mutations in gastrointestinal stromal tumors. Science. 2003 Jan 31;299(5607):708-10. Epub 2003 Jan 9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12522257
- Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, Kawano K, Hanada M, Kurata A, Takeda M, Muhammad Tunio G, Matsuzawa Y, Kanakura Y, Shinomura Y, Kitamura Y. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science. 1998 Jan 23; 279(5350):577-80.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9438854
- Hirota S, Ohashi A, Nishida T, Isozaki K, Kinoshita K, Shinomura Y, Kitamura Y. Gain-of-function mutations of platelet-derived growth factor receptor alpha gene in gastrointestinal stromal tumors. Gastroenterology. 2003 Sep;125(3):660-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12949711
- Isozaki K, Terris B, Belghiti J, Schiffmann S, Hirota S, Vanderwinden JM. Germline-activating mutation in the kinase domain of KIT gene in familial gastrointestinal stromal tumors. Am J Pathol. 2000 Nov;157(5):1581-5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11073817
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1885736/
- Oudijk L, Gaal J, Korpershoek E, van Nederveen FH, Kelly L, Schiavon G, Verweij J, Mathijssen RH, den Bakker MA, Oldenburg RA, van Loon RL, O'Sullivan MJ, de Krijger RR, Dinjens WN. SDHA mutations in adult and pediatric wild-type gastrointestinal stromal tumors. Mod Pathol. 2013 Mar;26(3):456-63. doi: 10.1038/modpathol.2012.186. Epub 2012 Nov 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23174939

- Roskoski R Jr. Signaling by Kit protein-tyrosine kinase--the stem cell factor receptor. Biochem Biophys Res Commun. 2005 Nov 11;337(1):1-13. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16129412
- Wagner AJ, Remillard SP, Zhang YX, Doyle LA, George S, Hornick JL. Loss of expression of SDHA predicts SDHA mutations in gastrointestinal stromal tumors. Mod Pathol. 2013 Feb;26(2):289-94. doi: 10.1038/modpathol.2012.153. Epub 2012 Sep 7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22955521

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